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# Relationship between Insulin Secretory Function and Endogenous Hypertriglyceridemia in Obese Humans with Insulin Resistance

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MARUHAMA, Y., YANBE, A., ABE, R., OKUGUCHI, F., OHNEDA, A. and YAMAGATA, S. *Relationship between Insulin Secretory Function and Endogenous Hypertriglyceridemia in Obese Humans with Insulin Resistance.* Tohoku J. exp. Med., 1976, **119** (4), 357-367 —— Eighteen obese inpatients with insulin resistance revealed by i.v. insulin test and expressed in various grades of hyperinsulinemia and hyperglycemia were examined for plasma lipid levels. A significant positive correlation was found to be present between the plasma triglyceride (TG) level and the insulin response to glucose load. A stepwise multiple regression analysis revealed that the insulin secretory response, the plasma cholesterol level and the relative body weight contributed to the level of plasma TG. No difference was found in the grades of insulin resistance between patients with and without elevated TG. The ratio of sum of plasma insulin values to that of blood glucose values during glucose tolerance test was markedly increased in patients with elevated TG. The patients with relatively blunted insulin response and impaired glucose tolerance curves showed only slight hypertriglyceridemia. Endogenous hypertriglyceridemia in obesity seems to be more closely correlated with plasma insulin level, and therefore, with insulin action rather than insulin resistance. ——— endogenous hypertriglyceridemia; obesity; insulin resistance; hyperinsulinemia; insulin secretion

Decreased sensitivity to both endogenous and exogenous insulin, or insulin resistance, is one of the characteristics of obese humans with or without diabetes mellitus (Rabinowitz and Zierler 1962; Karam et al. 1963; Perley and Kipnis 1966; Reaven et al. 1970). Although this insulin resistance has been sometimes attributed to a certain change in adipose tissue (Salans et al. 1968), in the liver (Wahren et al. 1973) or in the global tissues, its exact etiology has not yet been established. Another abnormal feature frequently observed in obesity is deranged metabolism of endogenous triglyceride (TG); i.e., endogenous hypertriglyceridemia and hepatic TG accumulation (Maruhama et al. 1974, 1975). It is interesting that there are definite interrelationships among the levels of plasma endogenous TG released from the liver, liver TG, plasma insulin and over-all insulin sensitivity in non-

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diabetic obese humans (Maruhama et al. 1975). It is well-known that insulin resistance is usually accompanied by a compensatory elevation of plasma insulin (Karam et al. 1963; Perley and Kipnis 1966). It is also well recognized that insulin seriously influences synthesis (Topping and Mayes 1972; Tulloch et al. 1972) and turnover (Havel 1974) of endogenous TG. Thus, it is likely that elevated plasma insulin or insulin resistance is responsible for the deranged TG metabolism in obesity. Several authors suggested a close relationship between the elevations of plasma insulin and endogenous TG (Reaven et al. 1967; Ford et al. 1968; Bierman 1972); while Glueck et al. (1969) reported a different result. However, since those authors did not examine the insulin sensitivity, the possible role of insulin resistance in hypertriglyceridemia suggested by Havel (1974) could not be ruled out.

This study was performed in order to elucidate whether the elevated plasma insulin or insulin resistance itself is more significantly related to endogenous hypertriglyceridemia in obesity. For this purpose, obese subjects with similar grades of insulin resistance, but with wide ranges of hyperinsulinemia and glucose intolerance, were subjected for the investigations.

## Subjects and Methods

Eighteen inpatients, 12 males and 6 females, aged 30–60, who showed obesity (relative body weight>115%; see foot-note in Table 1) and insulin resistance were the subjects for this investigation. The patients who had diseases other than obesity or mild diabetes, which are known to complicate carbohydrate and lipid disorders, had been excluded. The clinical data of the patients is summarized in Table 1. Their relative body weights

Table 1. *Clinical data of obese patients with insulin resistance*

| Case No. | Name | Sex | Age (years) | RBW* (%) | Maximum RBW in past (%) | Age (years) of maximum RBW | Family history | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Diabetes | Obesity |
| 1 | HM | F | 58 | 141 | 185 | 54 | − | + |
| 2 | SH | F | 37 | 133 | 139 | 35 | − | − |
| 3 | ES | M | 59 | 116 | 128 | 46 | + | − |
| 4 | SM | M | 43 | 124 | 127 | 40 | − | + |
| 5 | SS | M | 39 | 118 | 125 | 35 | − | − |
| 6 | TH | M | 45 | 144 | 148 | 43 | + | + |
| 7 | SSa | M | 42 | 123 | 141 | 28 | − | + |
| 8 | MM | F | 50 | 131 | 159 | 35 | + | + |
| 9 | KK | F | 60 | 165 | 170 | 54 | − | + |
| 10 | RY | M | 31 | 125 | 136 | 30 | − | + |
| 11 | SK | M | 60 | 120 | 130 | 52 | − | − |
| 12 | NA | M | 31 | 157 | 160 | 30 | − | + |
| 13 | SY | M | 39 | 137 | 146 | 36 | + | + |
| 14 | HI | M | 39 | 126 | 139 | 38 | − | + |
| 15 | SO | M | 39 | 140 | 166 | 37 | − | − |
| 16 | SSu | M | 30 | 115 | 119 | 28 | − | + |
| 17 | TK | F | 49 | 136 | 146 | 47 | + | + |
| 18 | NT | F | 50 | 156 | 158 | 49 | + | + |

* Relative body weight, (actual body weight/standard body weight) $\times 100$. Standard body weight, (height in cm−100)$\times 0.9$ (kg).

corresponded to 115–165% of standard body weight. All patients had showed a gradual decline in their body weights during the past 1–15 years, though they had shown no acute weight change during the few months before admission. In 10 patients diabetes mellitus had been diagnosed 1–10 years before admission. A family history of diabetes was noted in 33% of the subjects, and this frequency was essentially the same in the subjects with and without diabetes. An incidence of obesity was high (72%) in the family history of those patients. They had been kept on the standard diet of 1800–2000 kcal per day (ca. 30 kcal/kg), containing 280–300 g of carbohydrate, 40–50 g of fat and 80–90 g of protein, for 2–3 weeks prior to this study. During those periods, various examinations had been carried out in order to rule out the diseases which are known to produce the secondary hypertriglyceridemia. Their body weights were maintained to within $\pm 0.5$ kg during those periods. No drugs which may affect the carbohydrate and lipid metabolism were used. After an overnight-fast, the blood specimens were taken from the patients for plasma TG (Van Handel and Zilversmit 1957), total cholesterol (TC) (Zak 1957), free fatty acids (FFA) (Itaya and Ui 1965) and lipoproteins (Lees and Hatch 1963). Then, an oral glucose tolerance test (OGTT) using 50 g of glucose was performed. In this test, the capillary and venous blood samples obtained before, and 30, 60, 90 and 120 min after the glucose loading were analysed for blood glucose (Huggett and Nixon 1957) and for plasma insulin (Morgan and Lazarow 1962). An intravenous insulin test was performed a few days after OGTT. In this test, blood glucose and plasma FFA levels were measured before, and 15, 30, 45, 60, 90 and 120 min after single i.v. injection of regular insulin (Isuzilin, Shimizu Pharm. Co., Shimizu; 0.1 U/kg). Insulin sensitivity index, the velocity of blood glucose fall in response to insulin, was calculated as the maximum blood glucose fall from the fasting level (mg/100 ml) divided by time (hr) to the maximum blood glucose fall after i.v. insulin. In order to test the validity of this index, 7 obese subjects with hyperinsulinemia and almost normal glucose tolerance were examined for the index before and after weight reduction. As shown in Fig. 1, weight reduction and amelioration of hyperinsulinemia was both accompanied by significant increase in the insulin sensitivity index in all cases. Since it is known that overweight and hyperinsulinemia are usually associated with corresponding decrease in insulin sensitivity of tissues, the parallelism of either body weight or plasma insulin level and insulin sensitivity index seems to qualify this index as a quantitative measure of tissue insulin sensitivity.

Determinations of plasma lipid levels, OGTT and intravenous insulin test were also performed on 15 normal subjects with an average age of $39 \pm 2$ years ($\pm$ S.E.) and relative body weight of $104 \pm 3$%. They had been on usual Japanese diet (2000–2400 kcal, high in carbohydrate) before the examinations.

Student's *t*-test (small smaple method) was used to examine statistical significance. Analysis of correlation and stepwise multiple regressioon analysis, with addition and deletion of variables and analysis of variance, were performed on a NEAC 2200-Model 500 computer at Tohoku University Computer Center. For these analyses, a logarithmic transformation was applied to some variables (see next session) in order to correct otherwise skewed distributions of the variables.

## Results

*Laboratory data* (Table 2)

Plasma TG levels varied from 75 to 604 mg/100 ml (average, 252 mg/100 ml). Plasma TC ranged 182–396 mg/100 ml (average, 251 mg/100 ml) and plasma FFA ranged 358–1625 $\mu$Eq/liter (average, 852 $\mu$Eq/liter). Except for 6 patients (cases Nos. 1–6), all patients showed an increase in prebeta lipoprotein band on paper-electrophoresis (Lees and Hatch 1963). The result was compatible with endogenous hypertriglyceridemia. Fasting blood glucose levels remained within the normal

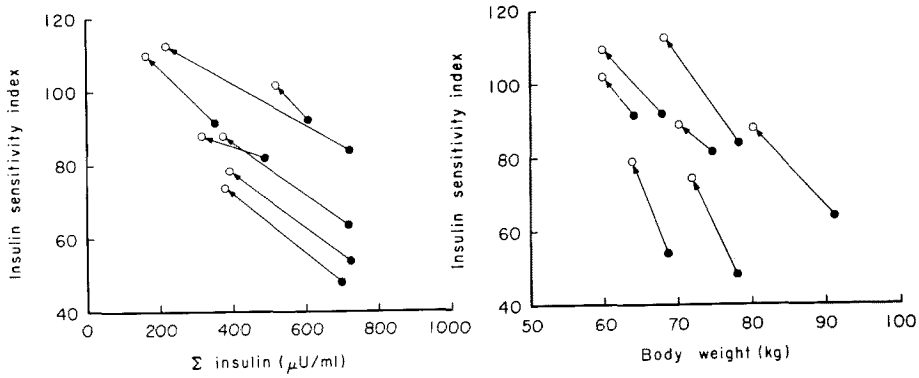


Fig. 1. Relationships between insulin sensitivity index and body weight or ΣInsulin before (●) and after (○) weight reduction in 7 obese insulin-resistant patients. Insulin sensitivity index, maximum blood glucose fall (mg/100 ml)/time (hr) to the maximum blood glucose fall after i.v. insulin injection. ΣInsulin, sum of 5 half-hourly plasma insulin values during oral glucose tolerance test.

range in a few patients, but those rose slightly in the other patients (average, 105 mg/100 ml). The sum of 5 blood glucose values during OGTT (ΣGlucose) ranged from 524 to 1131 mg/100 ml (average, 824 mg/100 ml). Basal plasma insulin levels were 6–56 μU/ml (average, 25 μU/ml), and the sum of 5 plasma insulin

TABLE 2. *Laboratory data of obese*

| Case No. | Plasma TG (mg/100 ml) | Plasma TC (mg/100 ml) | Plasma FFA (μEq/liter) | FBG (mg/100 ml) |
|---|---|---|---|---|
| 1 | 75 | 206 | 1012 | 108 |
| 2 | 76 | 210 | 929 | 140 |
| 3 | 79 | 246 | 954 | 117 |
| 4 | 95 | 212 | 1625 | 100 |
| 5 | 118 | 204 | 754 | 91 |
| 6 | 124 | 300 | 455 | 117 |
| 7 | 164 | 266 | 914 | 150 |
| 8 | 169 | 186 | 1250 | 112 |
| 9 | 192 | 275 | 442 | 107 |
| 10 | 202 | 182 | 574 | 98 |
| 11 | 223 | 235 | 358 | 131 |
| 12 | 247 | 252 | 551 | 80 |
| 13 | 299 | 290 | 1360 | 90 |
| 14 | 320 | 282 | 1009 | 91 |
| 15 | 477 | 280 | 797 | 91 |
| 16 | 480 | 258 | 887 | 87 |
| 17 | 587 | 244 | 891 | 101 |
| 18 | 604 | 396 | 569 | 86 |
| Mean | 252 | 251 | 852 | 105 |
| ±S.E. | ±41 | ±12 | ±79 | ±2 |

* Maximum blood glucose fall (mg/100 ml)/time(hr) to the maximum sum of 5 half-hourly blood glucose or plasma insulin values during FFA, free fatty acids. FBG, fasting blood glucose.

values during OGTT ($\Sigma$Insulin) ranged from 120 to 716 $\mu$U/ml (average, 401 $\mu$U/ml). All the above values were significantly deviated from normal ranges (see control values in Tables 5 and 6). The patients selected for this study showed a moderate or severe insulin resistance; i.e., the insulin sensitivity indices calculated from the rate of blood glucose fall after the insulin injection were lowered and ranged from 36 to 100 (blood glucose fall in mg/100 ml/hr). The mean value of this index was 71±2 (±S.E.), being significantly lower than that of the control subjects (162±22).

*Correlations between the variables* (Table 3)

Since this study aimed mainly at observing the relationship between insulin secretory response during OGTT and plasma lipids, the values of $\Sigma$Glucose and $\Sigma$Insulin were used for statistical analyses as indices of glucose tolerance and insulin secretion. In the analysis of correlations, a logarithmic transformation was applied to relative body weight as well as to plasma TC, FFA and TG. The transformation of these variables provided nearly normal distributions. There were significant positive correlations between the plasma TG level and $\Sigma$Insulin or plasma TC. A significant negative correlation was found between plasma TG and $\Sigma$Glucose. Plasma FFA was correlated with none of the variables. There were significant positive correlations between relative body weight and plasma TC or $\Sigma$Insulin. A significant negative correlation was found between $\Sigma$Insulin

*patients with insulin resistance*

| $\Sigma$Glucose (mg/100 ml) | Basal plasma insulin ($\mu$U/ml) | $\Sigma$Insulin ($\mu$U/ml) | Insulin sensitivity index* |
|---|---|---|---|
| 953 | 42 | 334 | 52 |
| 1127 | 18 | 150 | 80 |
| 1071 | 29 | 178 | 71 |
| 737 | 12 | 200 | 98 |
| 810 | 34 | 257 | 88 |
| 911 | 34 | 334 | 86 |
| 1131 | 20 | 120 | 37 |
| 1022 | 56 | 410 | 61 |
| 805 | 24 | 232 | 100 |
| 700 | 6 | 602 | 88 |
| 1016 | 24 | 142 | 75 |
| 575 | 22 | 713 | 65 |
| 705 | 17 | 648 | 48 |
| 526 | 6 | 511 | 49 |
| 657 | 46 | 716 | 84 |
| 524 | 12 | 344 | 68 |
| 811 | 18 | 162 | 92 |
| 753 | 32 | 716 | 36 |
| 824 | 25 | 401 | 71 |
| ±46 | ±3 | ±52 | ±5 |

blood glucose fall after i.v. insulin injection. $\Sigma$Glucose or $\Sigma$Insulin, oral glucose tolerance test. TG, triglyceride. TC, total cholesterol.

TABLE 3. *Simple correlation coeficients between the variables in obese patients with insulin resistance*

| | ISI | ΣGlucose | ΣInsulin | TC | FFA | TG |
|---|---|---|---|---|---|---|
| RBW | −0.025 | −0.167 | 0.462* | 0.456* | −0.354 | 0.224 |
| ISI | | −0.049 | −0.206 | −0.397 | −0.208 | −0.197 |
| ΣGlucose | | | −0.659* | −0.275 | −0.008 | −0.616* |
| ΣInsulin | | | | 0.351 | −0.021 | 0.705* |
| TC | | | | | −0.269 | 0.554* |
| FFA | | | | | | −0.178 |

RBW, relative body weight. ISI, insulin sensitivity index. ΣGlucose or ΣInsulin, sum of 5 half-hourly blood glucose or plasma insulin values during oral glucose tolerance test. TC, total cholesterol. FFA, free fatty acids. TG, triglyceride.
* significant ($p<0.05$).

and ΣGlucose. No correlation was found between insulin sensitivity index and plasma TG.

*Multiple regression analysis* (Table 4)

This analysis was performed in order to clarify the complex interrelationships between the variables shown in the correlation analysis. Appropriate transformations of the variables were done as described in the correlation analysis. As shown at step 1, ΣInsulin was the variable most closely related to plasma TG. Plasma TC was taken as the second most closely related variable to plasma TG (step 2) and the multiple correlation coefficient was raised from 0.705 to 0.778 by the addition of this variable. The third variable which contributed to plasma TG was relative body weight (step 3). The multiple correlation coefficient was raised to 0.816 by the addition of this variable. The prediction equation for plasma TG as a function of ΣInsulin, plasma TC and relative body weight could account for 67% of the total variance of plasma TG. Plasma FFA, ΣGlucose or insulin sensitivity index was evaluated as less significant variables for plasma TG. Indeed, the

TABLE 4. *Stepwise multiple regression analysis with plasma triglyceride as dependent variable*

| Step | Variables in equation | Multiple correlation coefficient ($R$) | $R^2$(%)* |
|---|---|---|---|
| 1 | ΣInsulin | 0.705 | 49.8 |
| 2 | ΣInsulin, plasma TC | 0.778 | 60.5 |
| 3 | ΣInsulin, plasma TC, RBW | 0.816 | 66.6 |
| 4 | ΣInsulin, plasma TC, RBW, plasma FFA | 0.832 | 69.2 |
| 5 | ΣInsulin, plasma TC, RBW, plasma FFA, ΣGlucose | 0.840 | 70.6 |

* Percentages of total variance of plasma triglyceride accounted for by the prediction equation of each step. ΣInsulin or ΣGlucose, sum of 5 half-hourly plasma insulin or blood glucose values during oral glucose tolerance test. TC, total cholesterol. RBW, relative body weight. FFA, free fatty acids.

multiple correlation coefficients as well as $R^2$ values showed only small elevation, even if such variables were added to the equation as shown at steps 4 and 5. However, there was a significant negative correlation between ΣGlucose and plasma TG or ΣInsulin. Therefore, it is likely that the negative effect of ΣGlucose upon plasma TG was an indirect one, and the rise in ΣGlucose in the insulin resistant patients was attributed to the relative decrease in ΣInsulin, the insufficiency of insulin secretory function.

*Comparison of insulin secretory function between the patients with and without elevated plasma TG* (Tables 5 and 6)

Clinical and laboratory data of the two patient groups, one with relatively low plasma TG (<200 mg/100 ml) and the other with high plasma TG (>201 mg/100 ml), were compared. There were no differences in age, relative body weight, insulin sensitivity index, plasma TC or FFA between the two patient groups, as shown in Table 5. The patients with high plasma TG levels showed significantly lower levels of fasting blood glucose as well as ΣGlucose, and significantly higher levels of ΣInsulin and insulin response index than the other patient group, as shown in Table 6. It is to be noted that the hypertriglyceridemic group showed an insulin response index more than twice as high as that in the control group. It is also noteworthy that the basal insulin as well as ΣInsulin in the group with relatively low plasma TG were higher than those of the control group.

## Discussion

The present study demonstrated an important role of insulin secretory response in endogenous hypertriglyceridemia of obese, insulin resistant patients. The obese subjects without insulin resistance, hyperinsulinemia and glucose intolerance did not show an elevation in plasma endogenous TG (unpublished

Table 5. *Age, relative body weight, insulin sensitivity index and plasma lipids in normal subjects and in the patients grouped by plasma triglyceride levels*

| Groups | Age (years) | Relative body weight (%) | Insulin sensitivity index* | Plasma TG (mg/100 ml) | Plasma TC (mg/100 ml) | Plasma FFA (μEq/liter) |
|---|---|---|---|---|---|---|
| Normal subjects ($N$=15) | 39±2 | 104±3 | 162±22 | 82±6 | 180±20 | 514±28 |
| Obese patients Plasma TG <200 mg/100 ml ($N$=9) | 48±3 | 133±5[a] | 75±7[a] | 121±14[a] | 234±12[a] | 925±116[a] |
| Plasma TG >201 mg/100 ml ($N$=9) | 41±3 | 135±5[a] | 67±6[a] | 382±49[a,b] | 269±18[a] | 777±95[a] |

* See foot-note for Table 2. TG, triglyceride. TC, total cholesterol. FFA, free fatty acids. Figures express mean±S.E. a, significantly ($p$<0.05) different from normal subjects. b, significantly ($p$<0.05) different from the patients with plasma TG<200 mg/100 ml.

TABLE 6. *Responses of blood glucose and plasma insulin to oral glucose load in normal subjects and in the patients grouped by plasma triglyceride levels*

| Groups | Fasting blood glucose (mg/100 ml) | ΣGlucose (mg/100 ml) | Basal plasma insulin (μU/ml) | ΣInsulin (μU/ml) | Insulin response index (ΣInsulin/ΣGlucose) |
|---|---|---|---|---|---|
| Normal subjects ($N=15$) | 83±2 | 527±12 | 15±3 | 184±17 | 0.35±0.03 |
| Obese patients | | | | | |
| Plasma TG <200 mg/100 ml ($N=9$) | 116±6[a] | 952±46[a] | 30±4[a] | 246±30 | 0.27±0.03 |
| Plasma TG >201 mg/100 ml ($N=9$) | 95±5[a,b] | 696±49[a,b] | 20±4 | 490±84[a,b] | 0.85±0.10[a,b] |

ΣGlucose or ΣInsulin, sum of 5 half-hourly blood glucose or plasma insulin values during oral glucose tolerance test. Figures express mean±S.E. a, significantly ($p<0.05$) different from normal subjects. b, significantly ($p<0.05$) different from the patients with plasma TG<200 mg/100 ml.

observation). Therefore, insulin resistance may cause hyperinsulinemia and hypertriglyceridemia simultaneously, when the insulin secretory function is sufficient. The present study also suggests that in the insulin resistant patients whose insulin secretion is relatively blunted and who show the mildly diabetic glucose tolerance curves, the plasma level of endogenous TG is rather low. There were no differences in the grades of insulin resistance between the patients with and without hypertriglyceridemia in the i.v. insulin test. Thus, elevated plasma insulin, rather than insulin resistance by itself, seems to be closely coupled with the level of plasma endogenous TG. Our previous report (Maruhama et al. 1975), in which the patients with diabetic glucose tolerance curve (Committee report 1970) were not included, could not indicate quantitative relationships between plasma insulin and TG. It is now clear that in the previous report (Maruhama et al. 1975) the patients with insulin resistance and normal or borderline glucose tolerance curve were mostly hyperinsulinemic and hypertriglyceridemic, and the ranges of both plasma insulin and TG were too small to demonstrate a possible relationship. The present study supports the results of Reaven et al. (1967), Ford et al. (1968) and Bierman (1972), because it showed positive correlation between hyperinsulinemia and hypertriglyceridemia. The recent extensive study of Olefsky et al. (1974) demonstrated the essential role of insulin resistance in hypertriglyceridemia in obesity. They measured insulin resistance by glucose, epinephrine and propranolol infusion technique, and confirmed the hypothesis of Reaven et al. (1967) that hyperinsulinemia based on peripheral insulin resistance leads to accelerated hepatic TG production and to hypertriglyceridemia. Though our method used for estimating insulin sensitivity was simple as compared with that of Olefsky et al. (1974), the present study nevertheless supports the view of Reaven et al. (1967).

Furthermore, it should be emphasized from the present data that the insulin secretory function of the pancreas is indeed closely related to hypertriglyceridemia, and also that bluntness of this function may rather benefit hypertriglyceridemia in cases of obesity. Insulin resistance would seem to play a certain important role in plasma TG turnover and therefore in hypertriglyceridemia (Havel 1974); in fact, the patients with insulin resistance but without hyperinsulinemia exhibited slight but significant elevation of plasma TG compared with controls. In spite of this result, the effect of insulin resistance does not seem to be essential so far as hypertriglyceridemia of obesity is concerned.

It is not clear whether the patients with relative insulin deficiency and diabetic glucose tolerance curve had ever undergone hyperinsulinemic and more strongly hypertriglyceridemic stage previously, and whether the insulin plethoric hypertriglyceridemic patients can be included in prediabetes. Since there are no convincing data at present as to the relationship between obesity and diabetes mellitus, it is impossible to assume a single disease entity in all insulin resistant patients. However, even if these patients could be classified into two different groups – one with diabetes, and the other without diabetes – there is no evidence of biochemical and hormonal differences other than those found in blood glucose and plasma insulin and lipids. No difference was found in plasma glucagon between obese patients without diabetes and with very mild diabetes such as those included in this study (Ishii, personal communication). And the elevated blood glucose level could not be held responsible for the normal plasma TG level of the obese diabetic patients. Thus, it is very likely that the blunted insulin secretion – rather than diabetic glucose tolerance – could account for the TG level of obese mild diabetics which was lower than that of obese non-diabetics.

Of interest is the report of Taketomi et al. (1975), who showed a parallel reduction of the islet insulin content, hepatic glycolytic and lipogenetic enzymes and plasma TG after streptozotocin treatment in the genetically obese mouse (KK strain). This mouse strain is known to have peripheral insulin resistance, hyperinsulinemia, glucose intolerance, increase in hepatic glycolytic and lipogenetic enzymes, fatty liver and endogenous hypertriglyceridemia (Matsuo and Shino 1972; Taketomi et al. 1973). These features closely resemble our findings in certain human obesity (Maruhama et al. 1975). Since insulin is known to induce the hepatic enzymes which take part in the synthesis of endogenous TG, it is possible that long-lasting hyperinsulinism in the liver is the principal offender in the deranged metabolism of endogenous TG. The report on the streptozotocin-treated KK mouse (Taketomi et al. 1975) suggests that the TG derangement is rather ameliorated with an artificial decompensation of insulin secretory function in the insulin resistant animal. This seems to support the suggestions from this study. Reaven and Reaven (1974) found recently that the numbers of particles of very low density lipoproteins (endogenous TG) in the Golgi complex of the hepatocyte were significantly reduced in the rat with chronic insulin deficiency produced by streptozotocin. They also indicated that the rate of secretion of endogenous TG into plasma from

the liver was significantly decreased in such rats (Reaven and Reaven 1974). These findings also suggest the important role of plasma insulin concentration in TG metabolism.

In the present study, the elevation of plasma TG was significantly correlated with that of plasma TC. This might indicate that the plasma TC level in obesity is elevated as a result of hypertriglyceridemia, since it is well-known that plasma low density lipoprotein, which is rich in cholesterol, is the metabolic product of very low density lipoprotein in plasma (Bilheimer et al. 1972). Finally, there were no correlations between plasma FFA and the other variables. A kinetic study is necessary to know the role of FFA in the lipid disorder, as plasma FFA is known to turn over quickly (Issekutz et al. 1967).

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